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Osteophytes and osteoarthritis progression. Effects of nonsteroidal antiinflammatory drugs

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There is controversy as to whether nonsteroidal antiinflammatory drugs affect the progression of osteoarthritis (OA) in humans. Most short-term studies of patients with OA are directed at the relief of symptoms and based on clinical measurements of changes in pain and/or function. The relief of pain is indeed the ultimate goal of any drug used in a frequent condition like OA.

As the evolution is slow and as the variability of the clinical status of OA patients is large, radiological assessment of affected joints seems to constitute an objective means for long-term evaluation. The most frequently measured parameters are the joint space (in order to assess the joint-space narrowing) and the size of osteophytes.

The European Group for the Respect of Ethics and Excellence in Science (GREES) recommendations for governmental registration and approval of drugs used in the treatment of OA have added the requirement that the drug not have a deleterious effect on the non-diseased contralateral joint; i.e., no deleterious effect on normal cartilage [1].

In animal models, it is methodologically convenient to demonstrate changes in the mechanical structure of cartilage. Several studies have shown a protective effect of several compounds on cartilage structure and on osteophyte progression [2, 3]. In the study of Williams and Brandt [2], benoxaprofen was shown not only to impair the development of osteophytes, but also to have potentially adverse effects on the normal cartilage, thus emphasizing the relevance of the GREES requirements [1].

The reproducibility of the radiological evaluation seems to be good enough to determine the changes with time and discriminate any therapeutic effect of drugs in groups of patients. This is particularly true when special techniques are used [5].

In most studies of OA (except for rapidly progressive OA), there is an inverse relationship between the progressive narrowing of joint space and osteophyte size. Osteophyte size increased significantly in the placebo-treated groups [5, 6]. In most studies using conventional X-rays, there was a non-significant trend to a slower progression of OA in the NSAID-treated group, as compared to the placebo group [6, 7]. However, the amount of bone reaction seen on the radiograph varies enormously as OA progresses. Solomon *et al.* have suggested to divide OA into hypertrophic and atrophic categories [8]. The osteophyte size is only increased in hypertrophic OA. A distinction should also be made between age-related small osteophytes at the joint margins producing some degree of squaring at the joint margin and OA osteophytes which are much larger. The exact role played by marginal osteophytes on reduction of varus-valgus instability in osteoarthritic knees is still unclear [9].

A therapeutic intervention aiming at blocking osteophyte development could therefore not be wise in every case. However, in most cases, the prevention of joint destruction will be paralleled with a smaller development of osteophytes. Several nonsteroidal antiinflammatory drugs, benoxaprofen as well as intraarticular triamcinolone have been shown to dramatically reduce the number and size of osteophytes, both in animal and in human studies. The therapeutic effect on osteophytes can therefore be used as a means for assessing the effects of therapeutic intervention on joint destruction.

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